MIP1 DNA polymerase of *S.cerevisiae*: structural similarity with the *E.coli* DNA polymerase I-type enzymes

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In this paper we predict the location and overall structural organization of the 3'-5' exonuclease and DNA polymerization domains corresponding to the mitochondrial MIP1 DNA polymerase (1). As shown in Fig. 1A, the three highly conserved regions Exo I, Exo II and Exo III recently described (2), that form the three-dimensional 3'-5' exonuclease active site of *E.coli* DNA polymerase I (pol I; 3), are present, as in other three DNA pols from *S.cerevisiae* (see Fig. 1A) and in a large number of prokaryotic and eukaryotic DNA pols (not shown; 2), in the N-terminal portion of the MIP1 DNA polymerase. However, MIP1 is the only yeast DNA pol sharing extensive similarities with the C-terminal portion of pol I and other related DNA pols, as those of *Streptococcus pneumoniae* (Spn), *Thermus aquaticus* (Taq), and bacteriophages T7, T5 and SPO2 (Fig. 1B). These shared sequences (spanning 295 aa in the MIP1 DNA polymerase sequence) are proposed to form, according to the X-ray structure of the pol I Klenow fragment (4), a conserved DNA binding cleft which contains the polymerization active site. Pol I residues directly implicated, either in dNTP binding (Lys 758, Tyr 766 and His 881; 5, 6) or DNA binding (Arg 690; 7), are also conserved in the MIP1 DNA polymerase sequence (stars in Fig. 1B). This enzyme, like prokaryotic DNA pols and in contrast with nuclear eukaryotic DNA pols, is resistant to aphidicolin and sensitive to ddNTPs (1). These facts, and the amino acid homology shown in this paper, indicate that the mitochondrial MIP1 DNA polymerase, according to the theory of the endosymbiotic origin of organelles, must be considered as a prokaryotic-type DNA polymerase.

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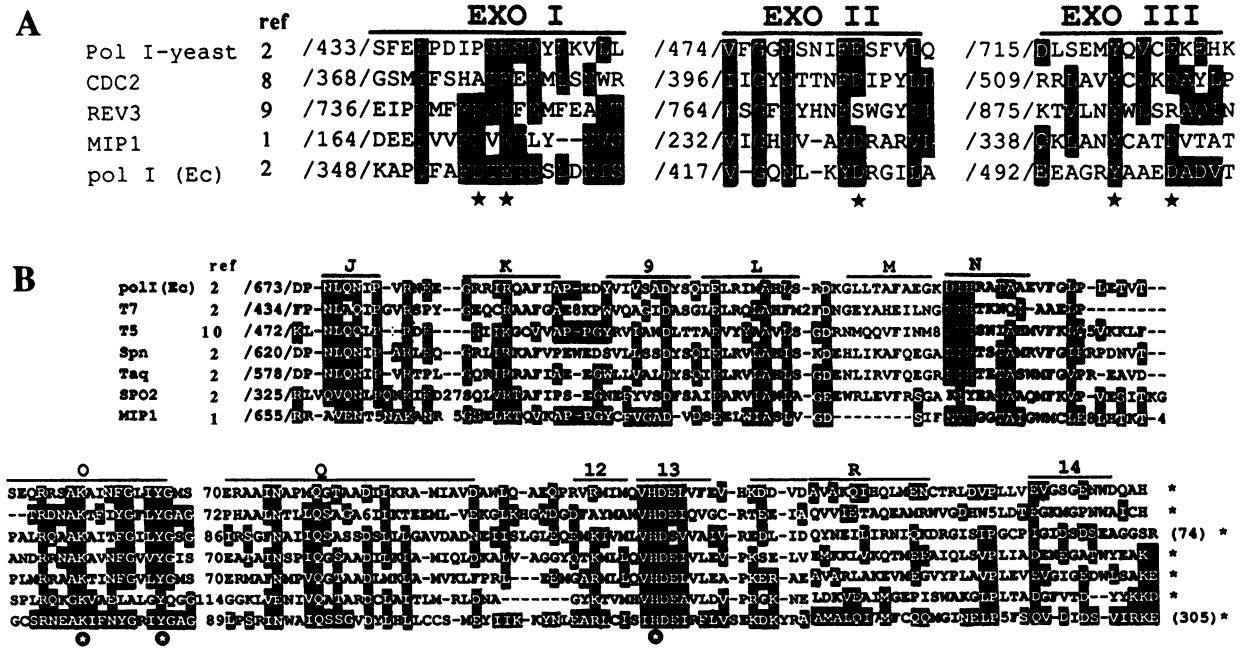

Figure 1. A. Predicted 3'-5' exonuclease domain in mitochondrial MIP1 and nuclear yeast DNA polymerases; stars indicate pol I (*E.coli*) residues involved in metal binding and exonucleolytic catalysis. **B.** Predicted polymerization domain of MIP1 DNA polymerase: amino acid sequence homology among MIP1 and prokaryotic pol I-type DNA polymerases. α-helices (lettered) and β-turns (numbered) are taken from the 3D-structure of pol I Klenow (4). Some original references are reviewed in reference 2.

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